REMARKS

With the present amendments, Claims 1-21, 23, and 25-29 are pending in the application, with Claims 1, 12, 21, 23, 25, and 28 amended and claims 30-32 canceled in this paper. The cancellation of claims 30-32 is without prejudice to the prosecution of the subject matter of these claims in related applications. The amendments to the claims find support in the specification and claims as originally filed. For example the amendments to Claims 1, 12, and 21 regarding the elements of the user facility find support in the specification and claims as originally filed, for example, at page 11, lines 16-18, and elsewhere in the application as filed. The amendments to Claims 1, 12, 21, 23, 25, 28, and 29 regarding a rate algorithm find support in the specification and claims as originally filed, for example, at page 13, lines 8-14; page 14, lines 13-28; page 15, lines 4-20; the original claims; and elsewhere in the application as filed. No new matter is added by way of the claim amendments.

Claims 1-21, 23, and 25-32 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Caple et al. (WO 99/04043, hereafter "Caple") in view of Kuga et al. (hereafter "Kuga"). Claims 1-21, 25-27 and 31-32 also stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Caple in view of Gulati et al. (U.S. 6,136,541, hereafter "Gulati"). Claims 23, 28, 29 and 30 further stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Caple in view of Hefti, U.S. Patent No. 6,338,968 (hereafter "Hefti).

Applicants traverse the claim rejections as discussed below.

Introductory Remarks

Applicant thanks the Examiner for his careful and thorough review and analysis of the present application and pending claims. Applicant realizes that the complexity of the claim language, necessitated by the subject invention, makes the examination of this application and these claims time-consuming, and applicant appreciates the effort and care that has been taken by the Examiner.

The Response to Arguments

The Examiner reviewed applicant's arguments on pages 2 and 3 of the Office Action mailed July 26, 2005. Applicant acknowledges with appreciation the Examiner's withdrawal of the rejection of claims 1-21, 25-27 and 31-32 under 35 U.S.C. § 112, 2nd paragraph. However, applicant believes that several of the Examiner's remarks bear further comment.

The Examiner notes that applicant "argues the combination of Caple and Kuga references fails to teach the use of peptide nucleic acid probes." This is correct. However, the Examiner goes on to remark that "a polypeptide encoded with DNA is described in Kuga's abstract and other various places in the patent document, and a polypeptide is a peptide, and the hybridization information collected from the DNA includes peptide." (page 2, lines 11-13). Applicant respectfully submits that this statement is incorrect, and does not accurately present the state of the art.

It appears that the Examiner is suggesting that the nucleic acid hybridization information provides sequence information sufficient to disclose the amino acid sequence of the polypeptide encoded by the DNA. However, as is made clear by the present amendments, the present invention uses levels of gene expression to diagnose the physiological condition of a patient. Furthermore, as discussed in the Amendment and Response mailed May 2, 2005, a "peptide nucleic acid (PNA)" is a specific kind of chemical, having a chemical nature and composition different and distinct from DNA. Thus, the PNA probes of the present invention being different and distinct from DNA probes, applicant reiterates that the combination of Caple and Kuga fails to teach the use of peptide nucleic acid probes.

The Examiner suggests that "Caple's system is capable of taking any test equipment ...." However, even if this were correct, applicant notes that Caple, in combination with Kuga, does not in fact disclose "any test equipment" that includes all of the elements of the present invention. The "nucleic acid probe analyzer" noted by the Examiner, mentioned in a reference that discusses DNA but fails to mention PNA or proteomics, is not "implicitly" a device that could be used for the present invention,

which is directed to systems having chips with PNA probes and proteomics probes. Accordingly, applicant reiterates that the combination of Caple and Kuga fails to teach all of the elements of the present invention.

The Examiner suggests that "even applicant admits the test data in the instant invention is insignificant to the system" since "the test data can be hybridization information of DNA or PNA probes." However, applicant respectfully points out that the portion of the specification referred to by the Examiner discloses a choice and not an statement that the test data is somehow "insignificant to the system." The present specification discloses a choice in the chemical entities that may be used as probes; the particular choice made will determine which of several disclosed systems have been chosen and will be used. However, since the PNA probes differ from the DNA probes, systems using PNA probes differ from systems using DNA probes. The present claims are directed to systems utilizing PNA probes and proteomic probes, which are disclosed in the specification along with the DNA systems noted by the Examiner in his remarks on page 2 and continuing on to page 3 of the Office Action mailed July 26, 2005.

In addition, the Examiner suggests that "the testing probes as to DNA or PNA should not carry significant patent weight in the instant invention." Applicant respectfully and strongly disagrees. Each element of a claim must be found in the prior art or in the knowledge of one of ordinary skill in the art. "In order to establish a prima facie case of obviousness, ... [t]he teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on the applicant's disclosure." *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). One cannot pick and choose elements of the claimed invention that may be ignored if they cannot be found in the prior art. As discussed above, and as discussed in previous Amendments, the use of PNA is an independent and significant element of the claimed invention. Moreover, PNA is not equivalent to DNA; it is more resistant to enzymatic degradation, is more stable in the face of hybridization conditions that would render DNA probes unworkable, and has other advantages and differences that make systems and methods comprising PNA probes distinct from other systems and methods which

may use other probes such as DNA probes. Accordingly, applicant submits that the fact that many of the present claims are directed to systems and methods comprising PNA probes does and should carry significant patentable weight.

The Examiner discusses Gulati, U.S. Patent 6,136,541 as also discussing "PNA microarrays on a biochip," referring to the abstract of that patent. However, Gulati discusses a technique "for identifying mutations, if any, in a biological sample, from a preselected set of known mutations" (lines 1-2 of the abstract). However, the present invention is not directed to identifying mutations or to determining which, if any, of several possible mutations might be present in a sample. The present claimed invention uses PNA probes to determine gene expression levels and not to identifying mutations as discussed in Gulati. Such analysis is disclosed in the application as originally filed. See, for example, page 10, lines 25-26: "The extent to which the hybridized DNA or RNA attaches to each spot on the chip indicates the level at which a specific gene is expressed in the sample." See also page 13, lines 8-9: "The diagnosis processing for this chip is based on the expression levels for each of these gene sequences, using predefined rules to determine the likelihood of a set of identified diseases or cancers." See also, for example, page 16, lines 17-18, and elsewhere in the specification. Accordingly, applicant believes that Gulati in combination with Caple also fails to provide all the elements of the claimed invention.

The Examiner, in discussing proteomics chips, suggests that "once again, the examiner recognizes that the chip is just another test kit that does not carry significant patentable weight." Applicant respectfully submits that the proteomics chips of the present claimed methods are not insignificant, but instead are elements of the claimed invention that cannot be summarily ignored. The use of proteomics chips, instead of other chips constitutes a choice that carries with it the concomitant properties and advantages of the chosen devices, which provide advantages and properties distinct from those of other types of chips. In addition, the present claims directed to proteomics also include analysis steps not discussed in the prior art cited by the

Examiner. Accordingly, applicant believes that Hefti in combination with Caple also fails to provide all the elements of the claimed invention.

The Rejections Under 35 U.S.C. §103(a) over Caple in view of Kuga

Claims 1-21, 25-27 and 31-32 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Caple et al. (WO 99/04043, hereafter "Caple") in view of Kuga et al. (U.S. 5,936,078, hereafter "Kuga"). Claims 31 and 32 standing canceled in the present amendment, it is believed that the rejections to claims 31 and 32 are moot.

In order to establish a prima facie case of obviousness, there must be: 1) some suggestion or motivation in the art or in the knowledge generally available to one of ordinary skill in the art, to modify or to combine the reference teachings; 2) there must be a reasonable expectation of success; and 3) the prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on the Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Peptide Nucleic Acid Microarray Claims

Claims 1-21, and 25-27 are directed to systems and methods which require, among many other elements, the elements of a microarray comprising peptide nucleic acid (PNA) probes comprising about 25 to about 70 bases in length tethered to a microarray surface. As discussed previously, a peptide nucleic acid (PNA) molecule is chemically and structurally different than a DNA molecule.

Applicants note that neither of the cited references discuss or suggest PNA molecules, or PNA microarrays, or the use of PNA molecules in any manner. Caple mentions only DNA (*e.g.*, page 10, line 19), not PNA, and Kuga make clear that their methods are directed to DNA molecules. For example, Kuga state that they "have developed high-density cDNA filter analysis" (Kuga, col. 2, lines 18-28). Unlike a PNA probe, cDNA is made from an RNA template. Moreover, cDNAs are not 25 to 70 bases long, but are often many hundreds or thousands of bases long, significantly longer than the about 25 to about 70 base-long probes of the present invention. Thus, Kuga

teaches away from the present invention by requiring cDNA molecules, unlike the PNA molecules of the claimed invention.

Applicants thus submit that Caple and Kuga fail to discuss or suggest PNA molecules or their uses. As acknowledged by the Examiner (see, *e.g.*, page 5, lines 16-22), Caple does not disclose this element of the claimed invention, among many other elements lacking from Caple. Kuga also fails completely to make up this lack, failing to include any reference to PNA molecules, PNA microarrays, or their uses.

Furthermore, the combination of Caple with Kuga fails to provide or suggest a PNA probe comprising about 25 to about 70 bases in length and fails to provide or suggest a PNA probe tethered to a microarray surface. Accordingly, Caple combined with Kuga fails to make obvious these claim elements as well.

Thus, the combination of Caple with Kuga fails to provide these elements required by the claimed invention, and so for this reason the combination of Caple with Kuga fails to make obvious the claimed invention.

The Length of the Probe

Caple in view of Kuga fails to provide the element of a probe of about 25 to about 70 bases in length. Applicant notes that the Examiner acknowledges that Kuga does not teach the claim element of probes comprising about 25 to about 70 bases in length tethered to a microarray surface (page 5, lines 7-12). Applicant notes that an acknowledgement that the prior art does not teach a claim element indicates that the claim element is novel; where the prior art also fails to suggest that element, it is not obvious.

However, the Examiner suggests (page 6, lines 3-4) that "the length of the probes tethered to a microarray surface" is "a matter of obvious design choice" without any supporting reference to indicate why he believes this to be so. In response to this assertion, applicant submits references showing that the intensity, sensitivity, and specificity, among other attributes, of a gene expression signal detected by hybridization to probes tethered to a surface are indeed affected by probe length, that the choice of a range of probe lengths is not consistent among references, and thus is not an obvious design choice but instead a distinguishing element of the claimed invention.

Probe length affects the accuracy and sensitivity of hybridization results. Kothapalli et al. (BMC Bioinformatics **3**:22 (2002)) noted that "Low specificity of probes is also a frequently encountered problem in oligonucleotide arrays" (page 2, column 2, lines 23-24). Their data confirmed the existence of the problem: "For example, the 1.2kb fragment (GB accession No.M 57888) spotted on the cDNA microarray as granzyme B was not able to distinguish between *granzyme B* and *H*" (page 2, column 2, lines 28-31). (A "1.2kb fragment" is a 1,200mer probe.) Such lack of sensitivity would make cDNA arrays unsuitable for use in systems and methods for diagnosing a physiological condition of a living organism or patient, and for recommending a treatment for that physiological condition.

Chen et al. (Microbial and Comparative Genetics **4**:116 (1999)) found that signal intensity from labeled oligos varied with oligo length (over the range from 30mer to 90mer) and found that the highest signal intensity was observed with 90mers for genes with high expression levels, while signal intensity was highest with 70mers for genes with mid to low levels of expression.

However, Relogio et al. (Nucleic Acids Research **30(11)**:e51 (2002)) found that increasing oligo length increased the proportion of mismatched hybridization ("a decrease in match/mismatch (M/MM) ratio was observed with the increase in oligo length" page 4, column 2, lines 5-7). They noted that "This trend is expected, as longer oligos are more likely to energetically accommodate a single nucleotide mismatch at a central position" (page 4, column 2, lines 9-11). In addition, Relogio et al. found a significant effect of oligo length on signal intensity for short oligos, in that the signal intensity of 30mer and 35mer oligos was more than double that for 25mer oligos.

In addition, Chou et al. (Nucleic Acids Research **32(12)**:e99 (2004)) studied probe lengths from 25mer to 1000mer, looking at signal intensity, the number of probes per gene needed for statistically significant gene expression measurements, and the effect of probe length on cross-reactivity (probe specificity). They concluded that, for their optimization criteria, the optimal probe length was 150mer.

Thus, although the art teaches that probe length affect the accuracy, sensitivity and reliability of hybridization measurements, there is no agreement in the art as to a

proper probe length for such measurements. The choice of an optimal length may depend upon the type of signal to be detected, the required specificity, the required signal intensity, the further analysis to be performed on such measurements, and will certainly involve skill in choosing a proper range where multiple types of signals may need to be measured.

Applicant has disclosed and claimed a range of probe lengths suitable for the practice of the invention. Applicant submits that the claim element of PNA probes comprising about 25 to about 70 bases in length tethered to a microarray surface is novel, as acknowledged by the Examiner, and is not obvious in view of the lack of teaching or suggestion of this element in the combined prior art references cited by the Examiner or in view of the prior art as a whole.

The Rate Algorithm

The claimed invention requires that hybridization information be analyzed with a rate algorithm that comprises detecting levels of gene expression (both high and low levels), and relating the gene expression levels with a patient's family history an organism's profile in order to determine the likelihood of developing a specific disease. Such an analysis is useful in diagnosing a physiological condition of the patient or living organism.

The combination of Caple and Kuga fails to provide such a rate algorithm, and fails to provide for the use of detecting high and low levels of gene expression, in conjunction with the family history of a patient or profile of an organism, in making a diagnosis of a physiological condition. Accordingly, Caple in view of Kuga fails to make the claimed invention obvious.

In addition, as discussed in the previous response, the combination of Caple in view of Kuga also fails to provide other claim elements as well. For example, the combination of Caple in view of Kuga fails to provide or suggest methods comprising updating hybridization parameters and profiles; Caple in view of Kuga fails to provide methods for diagnosing a physiological condition and recommending treatment

comprising collecting information from a PNA microarray, analyzing such information with a rate algorithm as discussed above, and updating stored parameters and profiles.

Moreover, there is no motivation or suggestion in the cited references that they be combined to provide a rate algorithm as discussed above and as recited in the claims, nor that they be combined to provide a PNA probe comprising about 25 to about 70 bases in length tethered to a microarray surface. Thus, the cited references do not provide any suggestion to be combined to provide the claimed invention.

Lacking disclosure or suggestion of these and other elements of the claimed invention, the combination of Cable and Kuga fails to provide any reasonable expectation of success for such a combination of elements. Accordingly, Applicants submit that the rejection of Claims 1-21 and 25-27 over Caple in view of Kuga are overcome.

Proteomics Claims

Claims 23, 28 and 29 are directed to methods for diagnosing a physiological condition comprising the use of a proteomics chip. As discussed previously, a proteomics chip differs from a PNA chip and from any sort of genomic analysis device in that it provides information regarding the *proteins* present in a sample, and not the genetic material which codes for the proteins. Thus, discussion of genomic methods is misdirected when applied to Claims 23, 28 and 29 which deal with proteomics.

Applicants note that the combination of Caple with Kuga fails to provide or to suggest proteomic devices, the gathering of proteomic information, or the use of proteomic devices in any methods. In particular, Caple with Kuga fails to discuss using a proteomics device in methods for diagnosing a physiological condition of an organism and for recommending treatment for said organism.

As discussed above, Caple combined with Kuga also fails to provide other claim elements, such as, for example, failing to provide or suggest methods comprising generating proteomics profiles, updating proteomics parameters, and applying a rate algorithm comprising detecting high protein levels, detecting low protein levels, relating said protein levels with stored disease models and living organism profiles to determine

a likelihood of developing a specific disease for diagnosing a physiological condition of said living organism. The combination of Caple with Kuga fails to provide methods for diagnosing a physiological condition and recommending treatment comprising collecting information from a proteomics chip wherein the methods comprise analyzing data using artificial intelligence comprising application of a rate algorithm as recited above.

Moreover, there is no suggestion or motivation in the cited references to combine Caple with Kuga in order to provide the missing elements, including but not limited to failing to suggest or motivate providing a proteomics chip. Lacking these elements and lacking any suggestion of them, Caple in view of Kuga also fails to provide any reasonable expectation of success for such a combination.

Further Remarks

Although the Examiner suggests that Caple "teaches using DNA sequences to find treatment for Alzheimer's disease" (page 6, lines 19-20) no such teaching is found in Caple, although Caple does mention cognitive testing on page 6, line 21. However, cognitive testing does not involve the use of DNA sequences. Moreover, Kuga discusses the use of human brain cDNA libraries (see, *e.g.*, column 3, lines 39-48) which indicates that autopsy tissue is used; such methods cannot be applied to the diagnosis of a physiological condition of a living patient, and certainly not for recommending treatment for the deceased patient from whose brain the tissue was taken. As discussed above, cDNA probes are not only chemically distinct from the PNA probes of the present invention, but are much longer than the about 25 bases to about 75 bases of the present invention, and have significant specificity problems (see, e.g., Kothapalli et al., as discussed above) that make them unsuitable for the practice of the present invention.

Referring to Claim 2, the Examiner suggests that Caple teaches data comprising "genetic pattern database data for chip ID" (page 7, lines 7-8) yet provides no citation for this teaching. Applicants have not been able to identify any such teaching in Caple.

Referring to Claims 1 and 8, the Examiner suggests that Caple provides encryption (page 4, lines 24-25 and page 8, lines 5-6), suggesting that "any communication within a network contains basic encryption." However, despite the

Examiner's comment, it is clear that Caple does not discuss or suggest encryption. Applicants submit that encryption, like all other claim elements, must be discussed in a reference in order to be provided by that reference. The cited references lacking any discussion of encryption, Applicants respectfully submit that the cited references fail to make obvious Claim 8.

Applicants note that the cited references fail to discuss PNA or proteomics. Thus, the Examiner's suggestion (page 9, lines 14-15 and page 10, line 13) in referring to Claims 16 and 21 that Caple and Kuga teach "hybridization information" is not directed to the present claims, since the cited references do not discuss or suggest hybridization to PNA or proteomic microarrays.

The Examiner cites the phrase "sequence listings" from page 10, line 19 of Caple to suggest that the cited references provide "genetic pattern processing" (page 9, line 21, referring to Claim 17). However, a sequence listing is known by one of ordinary skill in the art to be a listing, in order, of the nucleotides (for a nucleic acid molecule) or amino acids (for a protein) that make up a nucleic acid or protein. Sequence listings are used to identify and characterize a molecule. A pattern of genetic material (such as many nucleic acids present in a sample) would be needed for "genetic pattern processing." As these terms are used in the art, applicants respectfully submit that mere sequence listings do not provide "genetic pattern processing."

With regard to Claim 23, the Examiner (page 10, lines 20-21) notes that Kuga at column 3, line 45 discusses cDNA probes; however, the Examiner seems to imply that a discussion of cDNA probes might be relevant to the claim element "proteomics chip." However, as discussed above, a proteomics chip differs in significant ways from a cDNA probe, including its chemical structure, specificity, and mode of binding, and discussion of a cDNA in no way makes obvious the claim element "proteomics chip."

With regard to Claims 23, the Examiner cites Kuga at column 6, lines 5-9 to suggest that "a routine nucleotide sequencing method" is a rate algorithm (page 11, lines 2-3). It is unclear how a methods for determining the identifying chemical characteristics of a nucleic acid molecule could be the claimed rate algorithm. As discussed in the specification of the present application (page 20, lines 26-27) the "rate

algorithm allows for fast pattern matching in large rule set(s) by storing information about the rules in a network." Applicants respectfully submit that neither Caple nor Kuga, nor the combination of the two, provide a rate algorithm, and that this claim element is not made obvious by the cited references.

Accordingly, Applicants believe that the claims are not obvious over the cited references, that the combination of Caple and Kuga together fails to provide all missing elements of Claims 1-21, 25-27, and 31-32 and respectfully submits that the rejection of Claims 1-21 and 25-27 over Caple in view of Kuga under 35 U.S.C. §103(a) is overcome.

The Rejections Under 35 U.S.C. §103(a) over Caple in view of Gulati

Claims 1-21, 25-27 and 31-32 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Caple in view of Gulati. Claims 30-32 stand canceled in the present amendment, so that the rejections to claims 31-32 are believed to be moot.

The Examiner states that Caple discusses many elements, but acknowledges that "[h]owever, Caple does not explicitly disclose the test result is hybridization information, and wherein said hybridization information related to said patient comprises hybridization information collected from array comprising peptide nucleic acid probes comprising about 25 about 70 bases in length tethered to a microarray surface contacted with clinical sample related to said patient." The Examiner further acknowledges that "Gulati does not explicitly teach the probes comprise about 25 to about 70 bases in length tethered to a microarray surface" (page 12, lines 12-13). Thus, applicant notes that the Examiner has acknowledged that the combination of Caple in view of Gulati fails to explicitly teach at least these elements of the claimed invention, and so has acknowledged that the claimed invention is not obvious over Caple in view of Gulati.

The Examiner's suggestion that "it is inherent that a sample tissue to be analyzed at the nucleic acid level, the probes must be tethered to a microarray surface contacted with a clinical sample" is not correct, at least for the reason that the nucleic acid analyses discussed in Kuga et al., for example, did not utilize a tether, but instead

utilized "DNA dotted on filters to prepare the DNA filters" (Kuga, column 10, lines 51-52). Moreover, it is believed that nucleic acid analyses may be done with probes free in solution (and so not attached to any surface). Thus, it is not inherent that a probe must be tethered to a microarray surface contacted with a clinical sample.

More specifically, it is not inherent that a probe that is tethered to a microarray surface be a probe comprising about 25 to about 75 bases in length. The combination of Caple in view of Gulati fails to provide such a probe, and fails to provide such a probe tethered to a microarray surface. Accordingly, applicant submits that Caple in view of Gulati fails both explicitly and implicitly to provide this element of the claimed invention.

Caple lacks discussion of PNA or PNA microarrays. The Examiner presents Gulati as discussing "PNA microarrays on a biochip," referring to the abstract of that patent. However, Gulati discusses a technique "for identifying mutations, if any, in a biological sample, from a preselected set of known mutations" (lines 1-2 of the abstract). The present invention is not directed to identifying mutations or to determining which, if any, of several possible mutations might be present in a sample. The present claimed invention uses PNA probes to determine gene expression levels and not to identifying mutations as discussed in Gulati. Such analysis is disclosed in the application as originally filed. See, for example, page 10, lines 25-26: "The extent to which the hybridized DNA or RNA attaches to each spot on the chip indicates the level at which a specific gene is expressed in the sample." See also page 13, lines 8-9: "The diagnosis processing for this chip is based on the expression levels for each of these gene sequences, using predefined rules to determine the likelihood of a set of identified diseases or cancers." See also, for example, page 16, lines 17-18, and elsewhere in the specification. Accordingly, applicant believes that Gulati in combination with Caple also fails to provide all the elements of the claimed invention.

Moreover, neither Caple, Gulati, nor Caple in view of Gulati discusses a rate algorithm comprising detecting high gene expression levels, detecting low gene expression levels, and relating said gene expression levels with patient family history to determine a likelihood of developing a specific disease as required by the claimed

invention. Accordingly, Caple in view of Gulati also lacks these elements of the claimed invention.

Thus, Caple in view of Gulati lacks at least the elements of PNA microarrays, PNA probes comprising about 25 to about 75 bases in length tethered to a microarray surface, and a rate algorithm comprising detecting high gene expression levels, detecting low gene expression levels, and relating said gene expression levels with patient family history to determine a likelihood of developing a specific disease. For this reason at least, Caple in view of Gulati fails to make obvious the subject matter of claim 1 and its dependent claims, claim 21, and claims 25-27. Accordingly, applicant believes that the claims are not obvious over the cited references, that the combination of Caple and Gulati together fails to provide all missing elements of Claims 1-21 and 25-27 and respectfully submits that the rejection of Claims 1-21 and 25-27 over Caple in view of Gulati under 35 U.S.C. §103(a) is overcome.

The Rejections Under 35 U.S.C. §103(a) over Caple in view of Hefti

Claims 23, 28, 29 and 30 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Caple in view of Hefti. Claims 30-32 stand canceled in the present amendment, so that the rejection to claim 30 is believed to be moot.

The Examiner presents Hefti as discussing "the use of proteomics chips for diagnostic applications" and suggests that "the only difference between claim 23 and 21 is Claim 23 calls for a proteomics chip as a test kit rather than a PNA microarray." However, both Caple and Hefti, and Caple in view of Hefti lack any discussion of analysis comprising "detecting high protein levels, detecting low protein levels, and relating said protein levels with patient family history to determine a likelihood of developing a specific disease for diagnosing a physiological condition of said patient" as required by the invention of claims 23, 28 and 29. Moreover, not only lacking the claimed analysis, Caple in view of Hefti also fails to discuss "analyzing said information to generate a proteomics profile for said patient" as required for the claimed invention.

Thus, Caple in view of Hefti lacks at least the elements of 1) a rate algorithm comprising detecting high protein levels, detecting low protein levels, and relating said protein levels with patient family history to determine a likelihood of developing a specific disease for diagnosing a physiological condition of said patient, and 2) analyzing said information to generate a proteomics profile for said patient" as required for the claimed invention. For this reason at least, Caple in view of Hefti fails to make obvious the subject matter of claims 23, 28 and 29. Accordingly, applicant believes that the claims are not obvious over the cited references, that the combination of Caple and Hefti together fails to provide all missing elements of Claims 23, 28 and 29 and respectfully submits that the rejection of Claims 23, 28 and 29 over Caple in view of Hefti under 35 U.S.C. §103(a) is overcome.

CONCLUSION

Applicants respectfully requests consideration and allowance of all pending claims. The Examiner is invited to contact the undersigned attorney at the telephone number indicated below should he find that there are any further issues outstanding.

Please charge any fees, including fees for extension of time, or credit overpayment to Deposit Account No. **08-1641** referencing Attorney's Docket No. **25527-0005**.

Respectfully submitted,

Date: November 18, 2005

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